بسم الله الرحمن الرحيم

Endovascular infections induced glomerular dysfunction

By
Ahmed Bahy
MD internal medicine

Endovascular sources of infection include

- Infective endocarditis (native and prosthetic)
- Infected ICD
- Aortic root abscess
- Infected ventriculoatrial shunt
- Infected central venous catheter
- Infected arteriovenous shunt
- Infected endovascular stent

Infective endocarditis

- Incidence : 30 to 100 episodes per million patient/year .

- Despite improvements in therapeutic strategies, the fatality rate has not significantly decreased since the end of the 1970s; more than one-third of the patients will die within the first year of diagnosis(Thuny et al ,.2012)
- Acute renal failure is a common complication of infective endocarditis which occurs in approximately one-third of the patients (Conlon et al 1998)

Renal Complications of Bacterial Endocarditis

Renal dysfunction associated with bacterial endocarditis can occurs via :

(1) Immune complex deposition with glomerulonephritis,

(2) Antibiotic-induced acute interstitial nephritis

(3) Acute tubular necrosis secondary to toxin or volume depletion

(4) Emboli causing renal infarction

(5) Direct invasion of the parenchyma by the microorganism

(6) Thrombotic microangiopathy with cortical necrosis secondary to disseminated intravascular coagulopathy

The incidence of renal complications in IE

- The incidence of renal complications of bacterial endocarditis ranges from 2 to 60% in patients with bacterial endocarditis
- The incidence of renal insufficiency in endocarditis has deminished since the advent of effective antibiotic therapy.
- 15-25% of deaths in endocarditis were accompanied by uremia in the pre-antibiotic era, whereas less than 5% of deaths were due to uremia in the post-antibiotic era

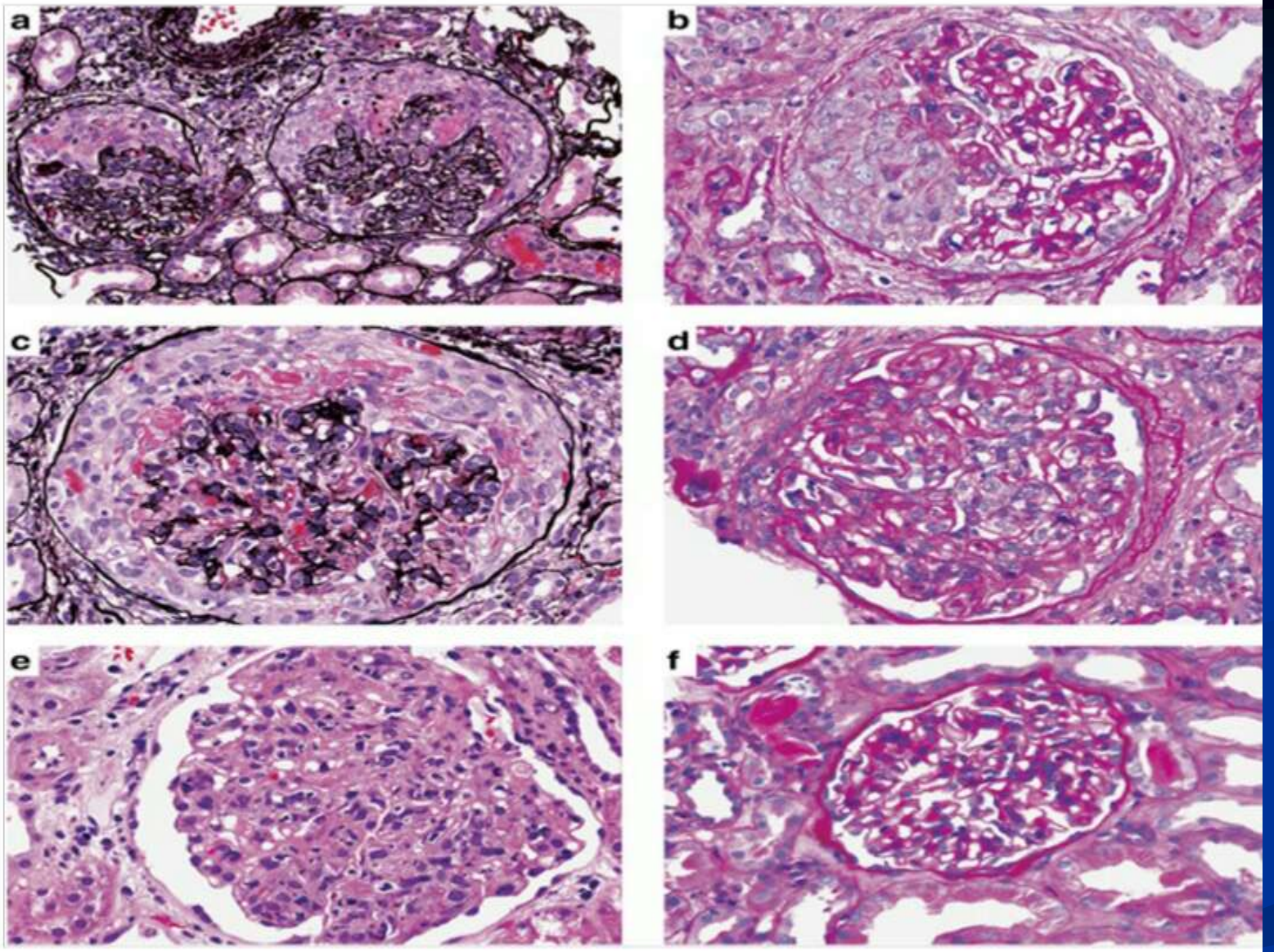
The renal pathology in IE

- The histopathological features of renal complications can be classified into three categories:

glomerular lesions, interstitial lesions, and both.

- Glomerular lesions vary from mild focal proliferative glomerulonephritis to diffuse necrotizing glomerulonephritis with crescent formation.

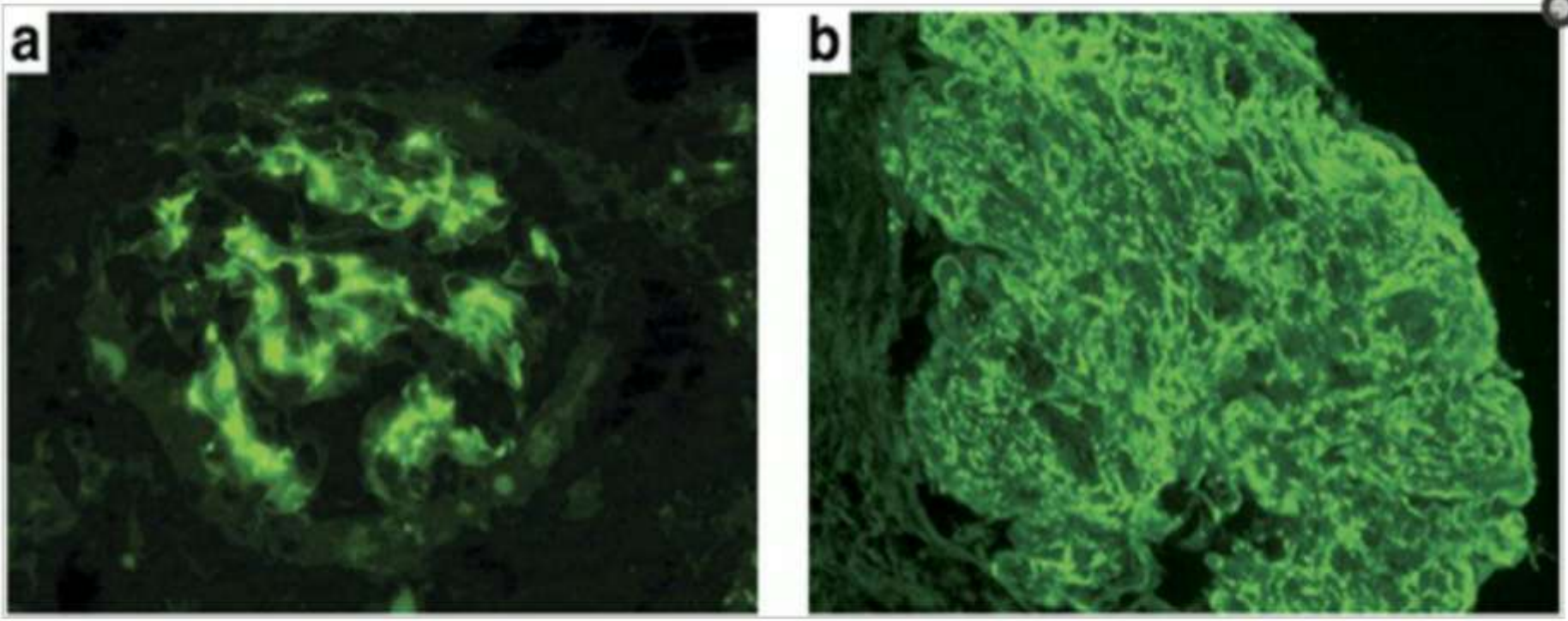
Glomerular lesions



Light microscopy findings in endocarditis-associated glomerulonephritis. (**a**) Cellular crescents with necrotizing foci (Jones methenamine silver; original magnification × 400). (**b**) Segmental cellular crescent with no underlying proliferation (periodic acid–Schiff; original magnification × 400). (**c**) Diffuse crescentic glomerulonephritis (Jones methenamine silver; original magnification × 400). (**d**) Acute focal proliferative glomerulonephritis (hematoxylin and eosin; original magnification × 400). (**e**) Diffuse proliferative glomerulonephritis (periodic acid–Schiff; original magnification × 400). (**f**) Mesangial proliferative glomerulonephritis (periodic acid–Schiff; original magnification × 400).

Kidney Int. 2015 Jun;87(6):1241-9

Figure 2



Immunofluorescence microscopy findings in endocarditis-associated glomerulonephritis. (**a**) Glomerulus with predominantly mesangial staining by C3 (fluorescein-conjugated anti-human C3; original magnification × 400). (**b**) Glomerulus with mesangial and capillary wall reaction with C3 (fluorescein-conjugated anti-human C3; original magnification × 400).

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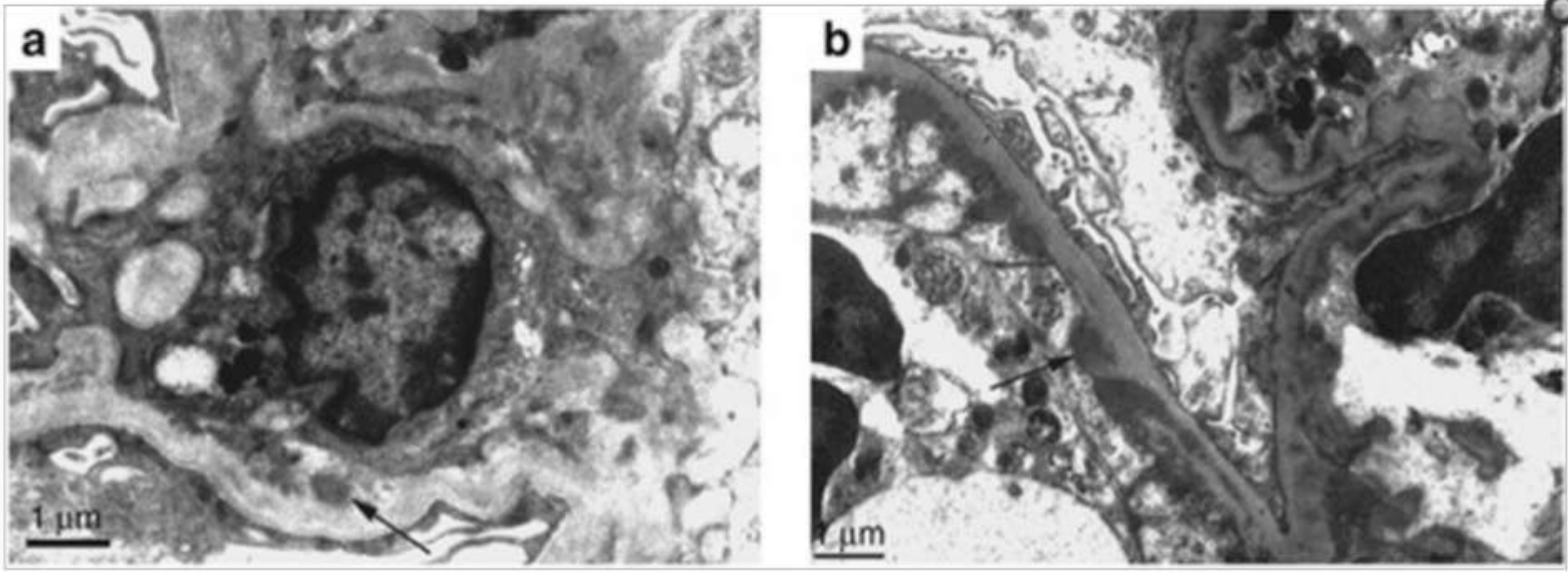
Figure 3



Electron microscopy findings in endocarditis-associated glomerulonephritis. (**a**) Mesangial electron-dense deposits (arrow) in diffuse crescentic glomerulonephritis (original magnification × 12,000). (**b**) Subendothelial electron-dense deposits (arrow) in focal proliferative glomerulonephritis (original magnification × 12,000).

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Interstitial lesions

- Acute interstitial nephritis and tubulointerstitial infiltration is often induced by beta-lactam antibiotics.
- Embolic renal infarction due to septic emboli shows fibrinous thromboemboli within artery with inflammation of the adjacent renal tissue. Thrombotic microangiopathy with cortical necrosis occasionally occurs in cases of severe septicemia associated with disseminated intravascular coagulopathy (DIC).

Laboratory Findings

- Urinalysis is usually abnormal.
- Proteinuria is the most frequent finding, being present in 50-80% on cases.
- Microscopic hematuria is seen in about 50% of cases.
- Gross hematuria indicates the presence of focal or diffuse glomerulonephritis or possible embolic renal infarction.
- Glomerulonephritis due to endocarditis typically present with urinary red blood cell casts and dysmorphic red blood cells.

- Eosinophiluria is a characteristic urinalysis finding of antibiotic-induced nephropathy. The finding of eosinophilia is relatively specific and possibly diagnostic for acute interstitial nephritis (sensitivity of 40%, specificity of 72%, and positive predictive value of 30%).
- Acute tubular necrosis can show a bland sediment or multiple granular casts, epithelial cell casts, and elevated urine sodium (Urinary Na>20mEq.

Pathogenesis of glomerular disease in IE

Immune-Complex Glomerulonephritis

Circulating immune complexes are present in 90% of glomerulonephritis due to endocarditis. In focal and diffuse glomerulonephritis, immunofluorescent studies reveal IgG, IgA, IgM and complement deposition along the capillary basement membrane and mesangium. IgG, IgM and IgA have been found single and incombination, together with complement. IgG is the most frequent immunoglobulin found . In contrast, serum IgE levels may be elevated in cases of antibiotic-induced acute interstitial nephritis

MRSA Glomerulonephritis

- For glomerulonephritis secondary to *Staphylococcal aureus endocarditis,* staphylococcal enterotoxins act as "superantigens" and bind directly to the MHC class stimulate resulting T cells to proliferate, camolecules of antigen-presenting cells and to the specific Vß chain of the T-cell receptor. These enterotoxins using massive activation of T cells and subsequent release of T cell derived lymphokines (e.g. IL-1, IL-2 and IL-6) and cytokines (e.g. TNF and INF-γ). Such cytokines cause polyclonal B-cell activation and immune-complex formation, resulting in glomerulonephritis

Antibiotics-Induced Nephropathy

- Antibiotics-induced nephropathy can affect each part of renal parenchyma including the glomerulus, proximal/distal tubule and interstitium, with or without inflammatory/ hypersensitivity process.
- The two major types of antibiotics-induced nephropathy are aminoglycoside-induced primary tubular necrosis
- drug-induced acute interstitial nephritis/tubulointerstitial nephritis.

Table 1: Renal Lesions Associated with Bacterial Endocarditis

	Frequency	Complement	Elevated Serum Ig	Pathology	Urinalysis	Clinical Course
Immune-complex glomerulonephritis	10-15% of IE	Low	IgG, IgM, IgA	Focal/diffuse glomerulonephritis	RBC casts Dysmorphic RBC	Improves after ABx
ABx-induced acute interstitial nephritis	+	Normal	IgG, IgM, IgA +/- IgE	Tubulointerstitial infiltration	+/-Eosinophils	Worsens after ABx
Embolic renal infarction	56% of the autopsy	Normal	None	Septic embolus in artery	Nonspecific	Variable
Renal abscess	Uncommon	Normal	None	Abscess	Nonspecific	Dependent on drainage
Thrombotic (DIC)		Normal	None	Thrombotic microangiopathy	Nonspecific	Variable
Acute tubular necrosis		Normal	None	Tubular necrosis	Granular casts, epitherial cell casts UNa>20mEq/L	Improves after supportive treatment
MRSA glomerulonephritis (superantigen-related nephritis)		Normal	IgA, IgG	Mesangial/endocapillary proliferative glomerulonephritis, tubulointestitial nephritis	Nephrotic range proteinuria	Improves after ABx

Ig: Immunoglobulin DIC: Disseminated Intravascular Coagulopathy

Infective endocarditis in renal transplant recipients

- Allograft rejection and infection remain major causes of morbidity and mortality following renal transplantation
- Approximately 30% of patients with end-stage renal disease may develop premature aortic and mitral valve calcification. In a small proportion of them, the calcification is severe and produces aortic or mitral stenosis. Premature aortic and mitral valve calcification is also frequent in dialysis patients and appears to be related to abnormal calcium and phosphate metabolism due to uncontrolled secondary hyperparathyroidism

- Several risk factors, such as frequent hospitalization, surgical and other invasive procedures, uremia, and extensive use of immunosuppressive therapy, make kidney transplant patients prone to infections in general and bacteremia in particular
- Infective endocarditis in patients undergoing renal transplantation and receiving immunosuppressive therapy may be difficult to diagnose
- A high index of suspicion is required to make the diagnosis.

Abstract

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Update on endocarditis-associated glomerulonephritis.

Boils CL[1], Nasr SH[2], Walker PD[1], Couser WG[3], Larsen CP[1].

Author information

Agent	Tricuspid (%)	Mitral (%)	Aortic (%)	Pulmonic (%)	Chordae (%)
Staphylococcus	76	31	50	50	0
Streptococcus	12	46	17	0	0
Other[d]	12	23	33	50	100

Kidney Int. 2015 Jun;87(6):1241-9

	Mean (range)
Light microscopy	
Total glomeruli	15 (2–43)
Sclerotic glomeruli	2 (0–16), 11% (0–87%)
	***n* (%)**
Glomerular pattern	
Crescentic	26 (53)
Focal	10 (20)
Diffuse	16 (33)
Necrotizing foci	20 of 26 (77)
Proliferative	18 (37)
Focal	2 (4)
Diffuse	16 (33)
Mesangial proliferative	5 (10)

Immunofluorescence microscopy	
Staining pattern	
Negative	3 (6)
Mesangial alone	20 (41)
Capillary wall alone	2 (4)
Capillary wall and mesangial	24 (49)

Electron microscopy			
Mesangial deposits			41 (84)
Subendothelial deposits			22 (45)
Subepithelial deposits			17 (35)
Subepithelial ‘humps'			7 (14)
No deposits			5 (10)

Shunt nephritis

- Shunt nephritis is an immune-complex-mediated glomerulonephritis (GN) associated with chronically infected ventriculoatrial shunts inserted for treatment of hydrocephalus. It was first described by Black et al. in 1965
- The initial event in shunt infection is colonization of the surface of the atrial part of the VA shunt, most commonly by a coagulase negative staphylococcal strain

- Staphylococcus species are res-ponsible for the majority of shunts' infections. *Staph. epidermidis accounts for about 40% and Staph. aureus for another 20% of all cases respectively* (Weprin and Swift,. 2002)
- Staphylococcus has a high affinity for the material of the shunt and produces a biofilm which protects the strains from the bactericide antibiotic
- Other bacteria of the normal skin flora such as gram positive cocci, gram positive anaerobic bacilli, gram negative bacilli or yeasts may also infect a ventricular shunt causing nephritis (Shapino et al., 1988)

- Negative blood or CSF cultures do not exclude shunt nephritis
- Decreased serum levels of complement, detection of cryoglobulins or autoantibodiesare helpful to support shunt nephritis diagnosis
- Intraglomerular deposition of circulating immune complexes and the subsequent activation of the classical pathway of serum complement's cascade result in glomerular inflammation

- Membranoproliferative gomerulonephritis is the most common histologic pattern observed in renal biopsy. The diagnosis needs high suspicion and is based on clinical and laboratory findings.
- Deterioration of renal function in association with signs of infection and low levels of serum complement's proteins C3 and C4 make the diagnosis possible.

Renal manifestations of shunt nephritis

- Microscopic or macroscopic he-maturia (88-100%), non-nephrotic range proteinuria (64-100%) or nephrotic syndrome (28-43%), arterial hypertension (10-64%) and renal failure (46-61%)
- Lab. Investigation
- Anemia, markers of inflamation, decreased complement , cryoglobulins, FR, proteinase 3 ANCA and culture

Renal pathology in shunt nephritis

- The membranoproliferative pattern is dominant in renal biopsy. Hypertrophic glomeruli with mesangial expansion and hypercellularity, duplication of the GBM and granular, mesangial, subendothelial or intramembranous depositions, predominantly of IgM, IgG and C3 are common findings. Pure mesangioproliferative lesions as well as endocapillary hyperplasia or extracapillary proliferation with crescents

- Shunt nephritis must be differentiated from subacute infective endocarditis,glomerulopathies with low serum complement levels such as poststreptococcal GN, lupus nephritis or C3 glomerulopathy as well as other seconda-ry causes of membranoproliferative GN (i.e. HCV-rela-ted cryoglobulinemic GN or light chain deposit disease).
- Although the initial colonization of the shunt usually occurs within the first months after the operation, glo-merulonephritis may develop after several months or even years

Take home message

High index of suspension is required in diagnosis of Endovascular infections induced glomerular dysfunction

Endovascular infections induced glomerular dysfunction Open field of researches


Thank
You!!